Evaluation of peripheral atherosclerosis: A comparative analysis of angiography and intravascular ultrasound imaging

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Objective: **Angiography remains a critical component for diagnostic imaging and therapeutic intervention in peripheral arterial disease (PAD). The goal of this study was to compare angiography with corresponding intravascular ultrasound (IVUS) imaging of the same vessels in patients with PAD.**

Methods: **From 2004 to 2008, 93 patients undergoing angiography for PAD were recruited in a prospective observational analysis. At the time of angiography, diseased lower extremities were interrogated using a 10-cm IVUS pullback with registration points. IVUS data were analyzed with radiofrequency techniques for vessel and lumen diameter, plaque volume, plaque composition, and cross-sectional area. Similarly, three vascular surgeons blinded to the IVUS data graded corresponding angiographic images according to vessel diameter, degree of stenosis, degree of calcification, and extent of eccentricity. Statistical analyses of matched IVUS images and angiograms were performed.**

Results: **The distribution of demographic and risk variables were typical for PAD: 54% male, 96% hypertension, 78% hyperlipidemia, 44% diabetic, 87% tobacco history, 65% coronary artery disease, and 10% end-stage renal disease. Symptoms precipitating the angiographic evaluation included claudication (53%), rest pain (18%), and tissue loss (29%). Angiographic and IVUS interpretation were similar for luminal diameters, but external vessel diameter was greater by IVUS imaging (7.0 ± 0.7 vs 5.2 ± 0.8 mm, $P < .05$). The two-dimensional diameter method resulted in a significant correlation for stenosis determination ($r = 0.84$); however, IVUS determination of vessel area stenosis was greater by 10% (95% confidence interval, 0.3%-21%, $P < .05$). IVUS imaging indicated that a higher proportion of plaques were concentric. Grading of calcification was moderate to severe in 40% by angiography but in only 7% by IVUS ($P < .05$).**

Conclusions: **In the evaluation of PAD, angiography and IVUS imaging provide similar luminal diameters and diameter-reducing stenosis measurements. Determination of overall vessel diameter and interpretation of plaque morphology by angiography are discordant from IVUS-derived data. (J Vasc Surg 2010;51:933-9.)**

Nearly 50 years after its invention, most vascular specialists still consider angiography to be the clinical gold standard for defining peripheral arterial anatomy.[1,2] Angiography is often used to corroborate stenoses severity documented by other imaging modalities, including ultrasound (US) imaging. However, angiography has many limitations. Angiography depicts arterial anatomy in a two-dimensional silhouette of the lumen that is dependent on the angle of image projection. Confounding factors include vessel tortuosity, obscure luminal shapes, concentric uniform lesions, and the evaluation of branch points. The resolution of angiography is further limited by the radiation exposure to the patient and arterial wall motion artifact. Despite these limitations, angiography remains the standard on which medical therapies, endovascular interventions, surgical bypasses, and clinical trials are based.

Advanced imaging modalities such as surface US imaging, computed tomographic arteriography, and magnetic resonance arteriography provide accurate arterial anatomy but are unable to define the structural components of the arterial wall. Intravascular US (IVUS) imaging, however, can provide high yield structural detail with improved resolution. We sought to compare standard digital subtraction angiography with IVUS imaging in patients being evaluated and treated for peripheral arterial disease (PAD). We compared angiography and IVUS imaging obtained from the same lower extremity arteries.

METHODS

This study was approved by the Cleveland Clinic Foundation's Institutional Review Board (No. 6723), and participants gave informed consent before enrollment.

Patient selection. This study design was a prospective observational study. Patients with chronic lower extremity ischemia undergoing lower extremity arteriography were recruited for participation. Inclusion criteria were symptoms of intermittent claudication, rest pain, or minor tissue loss (Rutherford category 1-5); ankle-brachial index (ABI) <0.9 in the affected lower extremity at rest or ≤ 0.80 after exercise in patients with resting ABI ≥ 0.90; and angiographic demonstration of a 100-mm patent segment of

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superficial femoral artery, common femoral artery, or external iliac artery with at least one visually estimated stenosis of >30% diameter reduction. Patients were excluded if they had acute limb ischemia, defined by a significant change in symptoms; contraindications to angiography; concurrent oral anticoagulant therapy that could not be safely withheld; or extensive tissue loss or gangrene. Baseline demographics, medical comorbidities, clinical presentation, and current medications were recorded.

Patients were offered enrollment from a single institution during the 4 years between 2004 and 2008, and data were collected in a prospective manner. A total of 93 were enrolled from a group of about 800 patients per year undergoing angiography with or without an intervention. This low number reflected the strictness of inclusion criteria mostly due to the requirement of a 100-mm patent vessel for imaging in the setting of PAD needing angiography and possible intervention.

Data acquisition. Angiography was performed with a fixed digital Angiostar angiographic system (Siemens AG, Munich, Germany), and original angiographic images were stored electronically (Magicview, Siemens AG). At the time of IVUS imaging, reference points were marked on angiographic images to directly compare the same 10-cm segment of artery. Three surgeons blinded to the IVUS results evaluated angiographic runs matched to the IVUS pullback. Angiographic images were selected for review that clearly delineated the diseased segments. Multiple planar images were not routinely obtained.

Evaluation of the angiograms included determination of proximal and distal diameters, diameter-reducing percentage of stenosis, stenosis concentricity (graded as concentric or eccentric), and grading of stenosis calcification. Stenosis percentage was determined by using the proximal adjacent healthy artery as the reference (1 – stenosis diameter/proximal diameter). Grading of calcium was scored on the following scale: none, minimal, moderate, and severe calcification.[3] Diameters and length of stenoses were reported in millimeters. Extent of atherosclerosis was categorized as involving <33%, 33% to 67%, and >67% of the analyzed segment.

During angiography, IVUS pullback was performed over a 10-cm segment with at least one >30% stenosis. All IVUS data were obtained using the In-Vision Gold IVUS console (Volcano Corp, Rancho Cordova, Calif), and the 3.5F Eagle Eye phased array IVUS catheter. The catheter tracks over a 0.014-inch guide wire system and has a 20-MHz US probe that produces a 20-mm field of view. During IVUS imaging, the catheter was advanced to the most distal aspect of the lesion, and then data were collected at a 1 frame/s using a Trak Back II, pullback device set at a motorized pullback rate of 0.5 mm/s.

Raw sequential radiofrequency (RF) IVUS data were saved and transferred to a workstation for analysis. Grayscale images were also acquired and assisted in the vessel contour definition process. Fiduciary points to aid in direct comparison of IVUS and angiographic images included branch points and matching of start/stop single fluoroscopic images. Of the 93 enrolled patients, 61 had directly comparable angiographic and IVUS images for analysis. Reasons for excluding IVUS imaging included the medial-adventitial border beyond the IVUS imaging field, poor resolution, lack of a complete 100-mm pullback, and other technical issues (n = 32).

Table I. Characteristics of the patients in the cohort

Variable	*Mean ± SD, or percentage (n = 93)*
Age, y	68 ± 10
Male	54
Hypertension	96
Hyperlipidemia	78
Diabetes	44
Smoking history	87
Creatinine, mg/dL	1.22 ± 0.8
End-stage renal disease	10
Presenting symptoms	
Claudication	53
Rest pain	18
Tissue loss	29

IVUS images were reconstructed from RF data using IVUS lab software.[4] Contours defining the internal elastic lamina and external elastic lamina of the vessel were identified automatically by the postprocessing software. Lumen and media-adventitial contours were then manually corrected for each gray scale image by a technician and reverified by another. IVUS analyses produced two distinct measurements for stenoses:

1. Diameter stenosis = 1 − lumen diameter/vessel diameter.
2. Area stenosis = 1 − lumen area/vessel area.

Atherosclerotic plaque composition was then computed using Volcano's Virtual Histology (VH) atherosclerotic plaque characterization algorithm. This tissue characterization is validated to a 10-mm field of view. Atherosclerotic plaques were characterized as fibrous, necrotic, or dense calcium. The output from the VH IVUS software yielded cross-sectional area information expressed in mm^2.

Statistical analyses. Patient variables are expressed as proportions for dichotomous variables and mean ± standard deviation for continuous variables. Differences between angiography and IVUS images were determined by the paired *t* test for parametric data. The χ^2 test was used for comparisons of nominal data, and the Fischer exact test was used when appropriate. To assess inter-rater concordance and agreement between angiography and IVUS, linear regression with Pearson product correlation coefficients were reported for parametric variables, and χ^2 test with Spearman rank correlation coefficients were reported for nonparametric data. Statistical significance was set at $P < .05$. All analysis was performed using SPSS 16.0 software (SPSS Inc, Chicago, Ill).

RESULTS

During the study period, 93 patients (54% men) were enrolled in the prospective study, and their characteristics are listed in Table I. Their mean age was 68 ± 10 years. The risk factors for atherosclerosis were prevalent in this popu-

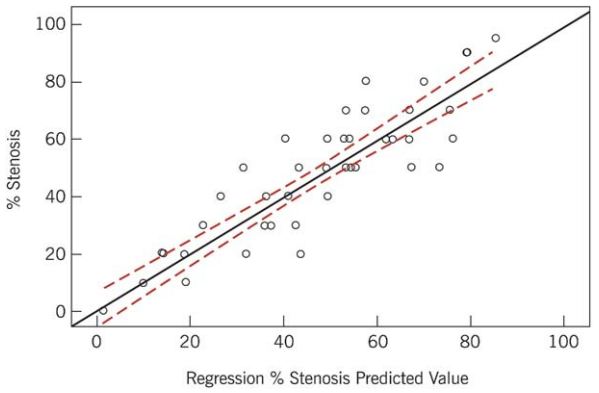

Fig 1. Inter-rater concordance is shown among angiographic examiners for determining maximal percent stenosis. The *open circles* represent actual measured data points among examiners, the *solid black* represents the linear regression through those points, and the *hashed red line* represents the 95% confidence interval.

lation, and 53% presented with claudication while the remaining patients presented with rest pain or tissue loss. The distribution of arteries analyzed included the common iliac artery, 7%; external iliac artery, 7%; superficial femoral artery, 73%; and the popliteal artery, 14%. The cohort primarily consisted of lesions in the superficial femoral artery, and 86% of those stenoses were located in the distal one-third of the superficial femoral artery.

Inter-rater concordance among angiographic examiners was evaluated using linear regression and calculation of Pearson correlation coefficients. The evaluation of 61 images for discrete angiographic measurements showed high inter-rater agreement for percentage of luminal stenosis ($r = 0.89$, Fig 1), proximal diameter ($r = 0.92$), and distal diameter ($r = 0.87$). However, the qualitative assessment of angiographic concentricity ($r = 0.26$), plaque calcification ($r = 0.64$), length of stenosis ($r = 0.66$), and extent of atherosclerosis ($r = 0.66$) yielded very poor inter-rater agreement among angiographic examiners.

To compare discrete measurements, a paired analysis was performed between angiographic and IVUS measures for diameters and maximal luminal stenosis (Table II). For both proximal and distal diameters, there was no significant difference in the assessment of actual lumen diameter in the vessel. Agreement between angiographic and IVUS luminal measurements was as high as 95%. Although only one vessel diameter can usually be assessed with conventional arteriography, IVUS determined both a luminal and outer wall diameter. Overall vessel size was approximately 1 to 2 mm larger than the luminal measurement at both locations. Likewise, luminal assessment of maximal stenosis was comparable for both angiography and IVUS, with good overall agreement. With IVUS, the maximal percentage area of stenosis was measured, and when compared with angiography, IVUS-derived degree of stenosis was greater by 10% (95% confidence interval [CI], 0.3%-21%; $P < .05$).

Plaque characteristics where compared in a similar fashion. Table III lists a paired assessment of length of stenosis, evaluation of concentricity, and estimation of calcification. By angiography, the length of stenosis was 14.3 ± 12 mm, but the same stenosis was 17.3 ± 13 mm by IVUS imaging, a 3.0-mm difference (95% CI, 0.9-5.1 mm; $P < .05$).

When determining the extent of calcification in a plaque, angiographic examiners found higher calcium burden within a lesion. Angiographic interpretation classified 40% of plaques as moderate or severe calcification, whereas IVUS evaluation only yielded 7% of patients meeting the criteria for moderate calcification and 0% for severe calcification ($P < .05$). In addition, angiographic examiners rated 72% of lesions as eccentric and the remaining 28% as concentric. In evaluating concentricity by IVUS technique, a plaque diameter index was used where >0.33 indicated a concentric lesion. By IVUS measurements, only 40% of lesions were eccentric and the remainder concentric.

Additional data obtainable only by IVUS imaging included plaque morphology and volume. Evaluation of the arterial segments with IVUS VH software determined that 63% of stenoses in this sample were primarily composed of fibrous plaque, 14% were classified as necrotic plaques, 9% had calcific plaques, and 14% were of mixed composition. Overall plaque burden for the area of pullback was 150 ± 44 mm^3/cm. This indicated the volume of plaque in the diseased arteries. The average cross-sectional areas for the vessel, lumen, and plaque were 30.7 ± 8.9 mm^2, 15.5 ± 6.4 mm^2, and 15.1 ± 4.7 mm^3, respectively. Fig 2 illustrates a an example of angiographic and IVUS analysis in a single vessel.

DISCUSSION

Contrast angiography is paramount for the evaluation and management of PAD, but it has significant limitations for evaluating atherosclerotic disease. The disassociation of angiographic findings and histologic analysis has been documented in both the coronary and peripheral vascular territories. Autopsy studies in patients who had undergone coronary angiography determined that 33% had coronary atherosclerosis that was unidentified by angiography.[5] In the peripheral vascular bed, we studied a select group of patients who had undergone angiography before amputation. The angiograms were compared with perfusion fixed arterial histology obtained from amputation specimens.[6] Angiography underestimated stenoses severity, arterial diameter, and was discordant from actual plaque architecture.[6,7]

Limitations of angiographic evaluation may account for the discordant results of treatment for PAD. In the treatment of femoral-popliteal disease, trials comparing medical therapy vs angioplasty for the treatment of claudication have failed to demonstrate a difference in symptom relief or walking distance during 2 to 6 years of follow-up.[8-10] This may reflect both recurrent disease and remnant occlusive disease that was not completely treated initially.

The Bypass Versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial compared surgical bypass with percutaneous transluminal angioplasty in the treatment of chronic limb ischemia due to infrainguinal disease. No demonstrable differences were identified in amputation-free survival.[11] However, technical failures occurred in 20%

Table II. A paired analysis of angiographic and intravascular ultrasound *(IVUS)* measurements in corresponding arterial vessel segments

Variable	*Angiographic analysis*	*IVUS analysis*		P[a]	r[b]
Proximal diameter, mm	5.5 ± 0.7	Lumen diameter	5.3 ± 0.9	.45	0.95
		Outer wall diameter	7.0 ± 0.7	<.05	0.28
Distal diameter, mm	5.2 ± 0.8	Lumen diameter	5.2 ± 0.9	.642	0.94
		Outer wall diameter	7.0 ± 0.7	<.05	0.31
Stenosis, %	46 ± 27	Diameter method	49 ± 25	.61	0.84
		Area method	55 ± 22	<.05	0.46

[a]Significance level of the paired *t* test for continuous variables and χ^2 analysis (or Fischer exact test where appropriate) for proportions.
[b]Correlation coefficient for the relationship between angiographic and IVUS measurements.

Table III. A paired analysis of angiographic and intravascular ultrasound *(IVUS)* assessments of plaque characteristics in corresponding arterial vessel segments

Variable	*Angiographic analysis*	*IVUS analysis*		P[a]	r[b]
Length of stenosis, mm	14.3 ± 12	17.3 ± 13		<.05	0.80
Calcification				<.05	0.27
None	26%	Calcium 0%-5%	51%		
Mild	33%	5%-15%	42%		
Moderate	28%	15%-25%	7%		
Severe	12%	>25%	0%		

[a]Significance level of the paired *t* test for continuous variables and χ^2 analysis (or Fischer exact test where appropriate) for proportions.
[b]Correlation coefficient for the relationship between angiographic and IVUS measurements.

of patients in the angioplasty arm and a high fraction of angioplasty patients required secondary procedures.

Lastly, the addition of self-expanding stents and stent grafts has improved the immediate angiographic result but has failed to demonstrate an improvement in long-term ambulatory status and amputation-free survival.[12-14]

We speculate that advances in intraprocedural imaging may aid in the performance and durability of endovascular therapies. Much of our understanding of peripheral atherosclerosis comes from studies in coronary arteries. IVUS imaging is a highly sensitive imaging modality that has been used to show a reduced rate of progression of atheroma burden in coronary vessels that could not be done using conventional angiography alone.[15]

In the present study, angiography was compared with IVUS imaging in the same arteries in patients presenting with PAD. Angiography and IVUS imaging provided concordant data on luminal diameters and maximal diameter stenoses. IVUS imaging provided additional information to include outer vessel diameter and maximal area stenosis. Given the irregular contour of the luminal surface, not all area stenoses were much greater than the diameter stenosis by IVUS imaging. For instance, a concentric narrowing will give an area stenosis larger than the diameter stenosis. On the other hand, a web-like stenosis may give a diameter stenosis larger than the area stenosis. Both measurement techniques give important information about the stenosis. The length of stenosis, plaque concentricity, and degree of plaque calcification determined by IVUS imaging were discordant to angiographic derived interpretation.

Angiographic luminal assessment is reliable but subject to error. The silhouette of a complex irregular lumen with calcium and thrombus superimposed poorly represents the actual lumen. Vessel movement and tortuosity further compound the luminal interpretation. In addition, angiograms cannot truly assess a disease-free reference segment for adequate comparison; a diffusely diseased artery may be interpreted as having no abnormalities. When the maximal diameter stenosis from angiography was compared with the maximal area stenosis from IVUS imaging, IVUS-derived data were greater by 10%. Also, when the overall length of plaque stenosis was determined, angiography-derived length of stenoses were 3-mm shorter than IVUS data. This difference in interpretation may account for some of the false-negative studies (33% to 39%) identified in postmortem histologic studies compared with angiography.[5,6]

Quantitative gray-scale IVUS images are limited by geometric measurements obtained by the end user or a software program, but limited objective information can be obtained from the echogenic interpretation of plaque characteristics. Qualitative assessment of echogenicity alone can be inaccurate due to the similarities of echogenicity between different tissue compositions: thrombus, lipids, fibrous, and calcific. Analyzing the raw RF data obtained from IVUS imaging allows the development of RF spectral profiles for different tissue types. This novel process, virtual histology, allows the objective classification of plaque morphology into the three primary categories of fibrous, calcific, and necrotic. This technology has most commonly been applied to the coronary vascular bed,[16,17] and the algorithm has been validated for carotid arteries.[18]

Qualitative variables assessed by angiography were different than IVUS-derived measurements. Plaque concentricity was much greater by IVUS imaging than by angiography. The

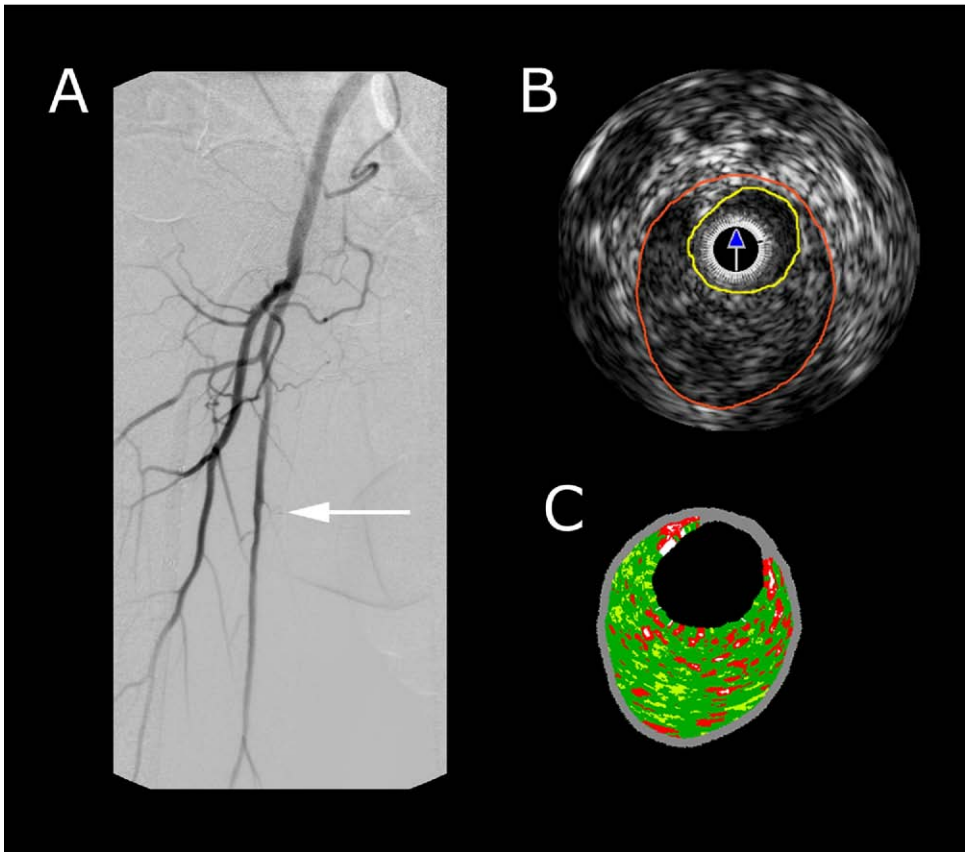

Fig 2. An example of angiographic and intravascular ultrasound (IVUS) analysis is shown. **A,** The *large white arrow* in the angiogram marks the area for analysis. This was interpreted as a 30% stenosis based on the angiogram. **B,** IVUS grey scale imaging through this area is illustrated. The *yellow line* marks the internal elastic lamina, and the *red line* marks the external elastic lamina. By IVUS, this represents a 76% area stenosis. **C,** In this example of virtual histology analysis, the *dark* and *light green shades* denote fibrous plaque, which accounts for the majority of this lesion, the *red areas* represent necrotic plaque, and *white areas* denote calcium.

high level of IVUS resolution provides information that is not comparable with angiography or any other surface imaging modality. Plaque morphology, including calcification, can be characterized by objective parameters with IVUS imaging and was less severe than estimated by angiography. Most lesions in this area were classified as fibrous by their RF profile. In a previous study, Bishop et al[7] identified increasing calcification with increasing distance from the popliteal artery irrespective of known clinical risk factors (diabetes, hyperlipidemia, and chronic kidney disease). In the present study, the superficial femoral artery comprised the majority of the population, and 44% of patients were diabetic, 78% were hyperlipidemic, and 10% had end-stage renal disease. The proximal vessels interrogated explain the relatively low percentage of calcific plaques observed in this study.

Despite the provocative results presented here, the clinical benefits of using IVUS imaging routinely and of plaque characterization in the periphery are largely unknown. This study highlights perhaps some of the limitations of angiography and illustrates the additional information obtained from IVUS interrogation. We are currently evaluating the clinical response to endovascular therapy in a larger cohort of PAD patients. It is foreseeable that particular plaque compositions may respond more favorably to endovascular intervention whereas certain subgroups should be reserved for surgical bypass. However, cost, additional operative/fluoroscopic time secondary to catheter exchanges, and additional equipment and personnel are additional hurdles that must be overcome for IVUS imaging to be used routinely.

Endovascular therapies are now routinely used as a revascularization modality in the lower extremities but suffer from limited durability.[11,14] Because most endovascular therapies are performed using angiography alone, unrecognized disease may cause decreased patency. Our study illustrates the difficulties of determining the beginning and end of disease with angiography, which may lead to inadequate treatment of the occlusive process. Furthermore, sizing of endovascular devices, including balloons for angioplasty and stents, are made by luminal rather than true vessel diameters. Thus, patients may return for treatment of remnant rather than recurrent disease.

Buckley et al[19] showed that IVUS imaging improved outcomes in patients undergoing iliac PTA and stenting. They concluded that IVUS imaging helped define arterial diameter and adequacy of stent deployment and led to improved patency and negating secondary procedures.[19] Whether routine IVUS usage during endovascular therapy would lead to improvements in treatment of infrainguinal disease remains unknown. More work in this arena is needed.

This study has some limitations that deserve mention. The small sample size subjects the study to potential unmeasured covariates and type II error. But given that this study was a paired analysis, we believe that a larger sample size would not affect our conclusions. The selected cohort somewhat limits the generalizability of the results. Despite a large clinical volume, we had difficulty enrolling patients into this trial. This is somewhat reflective of the strict inclusion and exclusion criteria, including the need for angiography and intervention, but with a patent 100-mm segment of lower extremity artery. In addition, the distal superficial femoral artery and popliteal artery comprised most of the data set; therefore, the results may not apply to the iliac or tibial vessels.

Angiography has been criticized for having poor interobserver reliability,[20] but in our study, inter-rater agreement was as high as 95% for discrete measurements between three surgeons. Because the complete media-adventitial border was not completely visualized by IVUS imaging, nearly one third of patients were excluded from analysis. This was largely experienced at the beginning of the study enrollment and in the larger arteries examined.

To decrease interobserver variability, software companies have designed programs, quantitative vessel analysis (QVA) software, that are intended to eliminate the examiner error with an objective, computer-based measurement. Unfortunately, these programs have the same limitations of conventional interpretation. QVA uses the lumenogram to obtain discrete diameters and calculate percentage stenosis. Inter-rater agreement was very poor for qualitative measurements of vessel concentricity, extent of calcification, and extent of atherosclerosis, and QVA would not be able to assess those variables. Given the high inter-rater agreement between angiographic examiners and the assumption that most vascular surgeons assess their own imaging, we do not believe that the addition of QVA would affect our results.

CONCLUSIONS

The evaluation and treatment of PAD depends on accurate angiographic imaging. Luminal quantitative assessments are very reliable with angiography, but assessment of true vessel diameter, actual area stenosis, plaque concentricity, and calcification are extremely discordant with IVUS imaging. In addition, IVUS imaging offers an objective assessment of plaque morphology. A better understanding of vessel and plaque morphology may identify parameters other than luminal flow-limiting stenoses in which to guide our therapeutic approach to PAD.

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DISCUSSION

Dr Peter Nelson (*Gainesville, Fla*). Dr Arthurs and his coauthors have scientifically brought to our attention the limitations of conventional angiography or what can be referred to as a 2D "lumenagram." From their data, intravascular ultrasound (IVUS) provides significant additional detail with respect to arterial morphology, specifically the measurement of true vessel outer wall diameter, area stenosis, and lesion length, all of which are underestimated by angiography, and importantly, information regarding plaque morphology and virtual histology that is simply unavailable from angiography alone. I offer the following technical and practical questions:

First, in your study angiography was accurate at predicting luminal diameters and importantly, maximal diameter stenosis. Isn't this enough information to make intraprocedural decisions regarding intervention, or do we need more information? For example, is the additional information that IVUS provides regarding full vessel diameter really necessary since it is standard practice to oversize stents and devices based on conventional angiography? Or, does the area of stenosis really add anything? The case example that you showed in your presentation I think is certainly telling, but if there is a false-negative on angiography, do you think that that lesion would turn out to be hemodynamically significant?

Second, with the increased capability and utility of noninvasive imaging such as CT [computed tomography] or MR [magnetic resonance] angiography (CTA or MRA), is some or all of this information potentially obtainable before performing angiography and therefore be potentially useful information for case-based planning?

Third, you point out that you had relatively few heavily calcified arteries in your study. Was this the result of case selection and/or do you have experience with calcified vessels and how does IVUS perform in that setting? Does shadowing or signal drop-out limit its utility in such cases?

Next, you have excluded chronic total occlusions in order to maintain the focus of the study, but do you have information as to whether there is any utility for IVUS in chronic occlusions and, if so, what information it provides?

And finally, can IVUS provide any hemodynamic information, either pressure readings or, more importantly, Doppler velocities or color flow measurements which would really provide added utility in determining the hemodynamic significance of stenotic lesions and then, in turn, ultimately guide the adequacy of your intervention.

Dr Zachary M. Arthurs. In regard to the first question, angiography provides a good luminal assessment. Does knowing the true vessel diameter and area of stenosis really matter? In order to understand the extent of atherosclerotic burden, I think the true vessel and area stenosis are important. In the example illustrated, the superficial femoral artery appears to be a reasonably healthy vessel by angiography, but it is truly diseased throughout the entire length. This accounts for significant underestimation of disease.

Are these lesions hemodynamically significant? Pressure measurements over long lesions are difficult to interpret. At this time, I would rely on noninvasive physiologic testing in order to determine their clinical impact. Based on the observation nature of the current study, I can determine the overall clinical impact of IVUS.

In the current state, surface imaging cannot obtain the resolution needed to assess the vessel wall in the periphery. Magnetic resonance imaging has been evaluated extensively in the carotid bed, and computed tomography in the coronary bed. In the periphery, it is very good for case planning, but I don't think it adequately assesses extent of disease.

In regard to the extent of calcification identified in our study, I think this is appropriate for the population studied. We have observed increasing calcification as you proceed down the peripheral tree, specifically in the tibioperoneal trunk and in the tibial vessels. Since our cohort was primarily superficial femoral artery lesions, I think this is an accurate finding. In addition, the angiographic evaluators, although experienced, overestimated calcification compared to IVUS.

Utilizing IVUS for chronic total occlusions poses several challenges. Placing the catheter in a subintimal plane vs through a central core will add variability to the interpretation. If predilation is needed in order to pass the 3.5F catheter, the images will be obscured as well. For these reasons, we have not utilized IVUS consistently for chronic total occlusions.

In my experience, I have not used IVUS to assess hemodynamic information. At the current time, flow velocities and pressure measurement are not able to be measured.

Dr Hasan Dosluoglu (*Buffalo, NY*). All the operators in this group were experienced, and although I thought that there was a 10% mismatch overall, the example you showed us was 74%. So what was the variation of the scores between the angiographic assessment and the IVUS assessment? What was the plus and minus standard deviation of that 10%? Which particular lesions were these very experienced operators particularly wrong? In other words, which type of vessels or lesions would IVUS be most beneficial to the interventionist?

Dr Arthurs. The example I gave you, of course, was an extreme example, 20% to 30%, to an area of stenosis of 76%. Even if you did a luminal calculation on that vessel I showed you, you would still probably get a 30% or 40% stenosis because it is diffusely diseased along the entire vessel and you are not using the true vessel diameter as your denominator to calculate the stenosis. On average, luminal diameter assessment underestimates the area of stenosis by 10%.

Angiographic evaluates were most discordant when it came to the qualitative assessment of the plaque. There was actually very good agreement on the luminal calculations of diameter and stenosis.

Dr Anil Hingorani (*Brooklyn, NY*). How much did it cost?

Dr Arthurs. Looking at the IVUS catheter itself, depending on your pricing that you are able to obtain, each individual catheter could be as low as $700 to as high as $1200, I've been told by some vascular surgeons that use them. On top of that, you have to buy or lease the actual hard drive, monitors, and software.

Dr Hingorani. Has this resulted in a change in your practice?

Dr Arthurs. Today, no. It makes me more conscious when interpreting peripheral angiograms and basing either endoluminal or surgical therapy.

Dr Hingorani. And finally, can you just go into a little more detail how 93 patients were selected out of 3200 patients, roughly?

Dr Arthurs. That illustrates the enrollment difficulties. The main enrollment barrier was identifying patients that had a patent vessel with an indication to undergo angiogram; and in addition, patient hesitation to consent for something that they otherwise would not have obtained if they weren't part of the study.

Dr Panagiotis Kougias (*Houston, Tex*). Most people would agree that one of the best applications of IVUS would be to assess the adequacy of an endovascular intervention in the SFA. Have you used this at all for this purpose?

Dr Arthurs. I have used it for that application, but only have anecdotal experience.

Dr Vikram Kashyap. I just wanted to put this study in context. This is part of an NIH [National Institutes of Health]-sponsored study. In this particular report we looked at the disparity between IVUS results and angiography in lower extremity lesions. We all know that there is a finite durability of our endovascular therapies. It may vary from institution, from the area of the vasculature treated, or from the modality that's used, but we all know that the durability is limited.

I think one takeaway message is often we don't treat restenosis, but what we treat is remnant disease that we didn't recognize initially.

The second point is that the virtual histology is a very compelling area. We hope to eventually get parameters that are predictive of success or failure. That is, highly calcific vessels may be better treated with one modality, such as atherectomy or cryoplasty, and perhaps fibrous lesions are better treated with another modality like stenting. We are not there yet, but that is the goal.